

REMARKS

Claims 1-3 and 5-21 are pending. Claims 3, 16, 17, and 19-21 are presently withdrawn from consideration. No amendments to the Specification or claims are made at this time.

Claims 1, 2, 5-15 and 18 stand rejected under 35 U.S.C. § 103(a) as being allegedly obvious over McIntyre et al. (Pharmacol. Ther., 74(2): 181-184 (1997), hereinafter "McIntyre") in view of Del Soldato (PCT Application Publication No. WO 00/61537, hereinafter "Del Soldato I") and Del Soldato (PCT Application Publication No. WO 95/09831, hereinafter "Del Soldato II"). This rejection is respectfully traversed.

Applicants note that the Examiner concedes that McIntyre does not teach or suggest attaching a nitroxy tether to losartan. However, the Examiner alleges that in view of the teachings of Del Soldato I, it would have been obvious to attach a nitroxy tether of Del Soldato II to losartan.

Applicants respectfully submit that attachment of the nitrooxy tether of Del Soldato I to the losartan of McIntyre would not have resulted in the compounds of the presently claimed invention. While Del Soldato I discloses that losartan is one of the many drugs that "can be used as precursors in formula (I) and (II)" (see, e.g., page 41 of Del Soldato), the use of losartan as a precursor in formula (I) or (II) of Del Soldato I would not result in the elected compound (i.e., compound 2 of the present application).

In particular, Applicants note that Del Soldato I discloses compounds of formula I $A-B-C-N(O)_s$. In formula I, $A = R-T_1$ and R is a radical of a precursor drug and -B-C- is a linker bridging the $-N(O)_s$ group and A. Further, B is represented as $-T_B-X_2-T_{B1}-$ and is an anti-oxidant moiety defined as a radical derived from a precursor molecule having

anti-oxidant properties. Thus, in contrast to the presently claimed compounds, Del Soldato I discloses compounds that comprise a precursor drug attached to the $-N(O)_2$ group via an anti-oxidant moiety B.

The Examiner alleges that because Del Soldato II teaches a direct attachment of a nitroxy tether to a drug such as naproxen, it would have been obvious to use the nitrooxy tether of Del Soldato II to make the presently claimed compounds. Applicants respectfully traverse this ground of rejection.

Del Soldato II is directed to nitric esters of propionic acid. Thus, Del Soldato II does not teach or suggest the presently claimed compounds. Furthermore, the compounds taught by Del Soldato II belong to a category of non-steroidal anti-inflammatory drugs whereas the presently claimed compounds belong to a category of angiotensin II receptor blocker. That is, the compounds of Del Soldato II and the presently-claimed compounds belong to different categories of medications with entirely different properties. Therefore, based on the teachings of Del Soldato II, a skilled artisan would not have been motivated to use the tether of Del Soldato II to obtain the presently claimed compounds.

Furthermore, the presently claimed nitrooxy derivatives of angiotensin II receptor blocker compounds show superior properties, such as improved vasorelaxation and anti-hypertensive activity, compared to the parent compounds. Table 1 of the Specification indicates that the NO-losartan of Examples 1, 2, 4, and 5 were able to induce vasorelaxation over a range of concentrations in contrast to the lack of vasorelaxation by losartan. Table 4 of the Specification discloses that the NO-losartan

of Example 2 was able to induce a greater reduction in blood pressure levels as compared to losartan over the treatment period.

Because McIntyre, Del Soldato I and Del Soldato II do not teach or suggest the compounds of the presently claimed invention or the unexpected advantages thereof, Applicants submit that the compounds of the presently claimed invention would not have been obvious to one of ordinary skill in the art over the disclosures of McIntyre, Del Soldato I or Del Soldato II, alone or in combination.

Furthermore, with respect to the elected compound, the nitroxy tether of the elected compound is $-\text{CO}-(\text{CH}_2)_3-\text{ONO}_2$ whereas the nitroxy tether disclosed by Del Soldato II is $-\text{O}(\text{CH}_2)_4-\text{ONO}_2$. Therefore, attachment of the nitrooxy tether of Del Soldato II to losartan as asserted by the Examiner would not result in the elected compound (i.e. compound 2) of the present application.

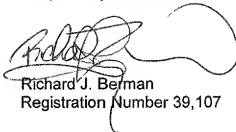
For at least the above reasons, Applicants submit that independent claims 1 and 15 are not obvious over the cited references. Because claims 2, 5-14 and 18 depend from independent claim 1, claims 2, 5-14 and 18 are also not obvious over the cited references. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 2, 5-15 and 18 under 35 U.S.C. § 103(a) over McIntyre in view of Del Soldato I and Del Soldato II.

CONCLUSION

For at least the above reasons, Applicant respectfully submits that this application is in condition for allowance and requests favorable action thereon. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicant's undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

In the event this paper is not considered to be timely filed, Applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, referring to Attorney Docket No. 026220-00073. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300, referencing Attorney Docket No. 026220-00073.

Respectfully submitted,



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